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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,299	01/26/2004	Gregory M. Lanza	532512001000	9201

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MORRISON & FOERSTER LLP
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EXAMINER

SCHLIENTZ, LEAH H

ART UNIT	PAPER NUMBER
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1618

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/18/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/765,299

Applicant(s)

LANZA ET AL.

Examiner

Leah Schlientz

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☒ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 January 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>4/12/04</u> . | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

Priority

It is noted that the priority date for the structure of the compound in claim 1 was determined to be the filing date of the 10/351,463 application, or 1/24/2003, for the purposes of searching prior art. The structure does not appear in the provisional application 60/351,390 filed 1/24/2002.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 – 23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain specific chemical moieties which represent R¹, including alkyl (1-6 C), halo, alkoxy (1-6 C), OR, NR₂, SR, CN, NO₂, SO₃H, and R, where R is alkyl or an alkenyl optionally substituted by halo, =O, and optionally containing O, S, or N (paragraph 42), it does not reasonably provide enablement for all possible “non-interfering substituents” as defined by broad functional language. The specification, while being enabling for certain specific chemical moieties which represent a spacer, such as CH₂CH₂, peptide, or polyalkylene glycol (paragraph 40), it does not reasonably provide enablement for a generic “spacer” as broadly claimed in claim 1. The specification does not enable any person skilled in the art to

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which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

- 1) the quantity of experimentation necessary,
- 2) the amount of direction or guidance provided,
- 3) the presence or absence of working examples,
- 4) the nature of the invention,
- 5) the state of the prior art,
- 6) the relative skill of those in the art,
- 7) the predictability of the art, and
- 8) the breadth of the claims.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth herein below.

The nature of the invention and the state of the prior art

The claimed invention relates to a compound represented by the structure of claim 1, including the variables R^1 and spacer, where R^1 is a non-interfering substituent. While the terms "non-interfering substituent" and "spacer" are recognized terms within the art, it is noted that the compound of claim 1 is a novel compound, which would require a degree of empirical determination regarding the nature of specific substituents which are "non-interfering" in the instant case, especially depending on the features of the chelate ligand and the length of the $(CH_2)_m$ variable.

The breadth of the claims, the amount of direction or guidance provided and the presence or absence of working examples

The claims are very broad and are inclusive of variables R^1 and spacer. R^1 represents any non-interfering substituent. This encompasses any substance which has that ability. However, the specification only teaches the use of certain specific organic functional groups to encompass the variables (such as alkyl (1-6 C), halo, alkoxy (1-6 C), etc.). The term "spacer" also encompasses any substance which has the ability to separate the chelate and the phospholipids moieties of the compound, but the specification only teaches the use of certain specific moieties which may perform the spacing function (i.e. CH_2CH_2 , peptide, or polyalkylene glycol), and does not provide guidance as to any other substances which may have that ability nor does the specification disclose any specific characteristics for other such substances. The specification provides direction or examples only for a specific few combinations of R^1 and spacer (i.e. examples 1 and 8).

The predictability of the art, the relative skill of those in the art, and the quantity of experimentation necessary

Given the great diversity between potentially available chemical groups to represent R^1 and spacer, there is a factor of unpredictability with regard to which combinations of any non-interfering substituent and any spacer that would be effective. Furthermore, without any information directing one to the desired structural properties of the spacer, one skilled in the art could not predict which substances out of the vast numbers of known substances would be appropriate. There is no screening method by

which to identify suitable compounds. Thus, a considerable amount of empirical testing is required with no *a priori* expectation of success by one of ordinary skill in the art in order to make and use the invention as claimed.

It is noted that the claims would be more favorably considered if the phrase "R¹ is a non-interfering substituent" were replaced with the specific limitations from the specification (paragraph 42), such as "R¹ is an alkyl (1-6 C), halo, alkoxy (1-6 C), OR, NR₂, SR, CN, NO₂, SO₃H, and R, where R is alkyl or an alkenyl optionally substituted by halo, =O, and optionally containing O, S, or N" for example, and a limitation such as "wherein spacer represents CH₂CH₂, peptide, or polyalkylene glycol" were included in claim 1.

Claims 1 – 23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The factual inquiries that have been considered include:

- physical and / or chemical structure
- functional characteristics
- correlation between structure and function
- method of making
- the representative number of species

Claims 1 and the respective dependent claims are drawn to a compound represented by the structure of Figure 1, including the variables R¹ and spacer, where

R^1 is a non-interfering substituent. A few specific examples of suitable chemical groups which may act as a "non-interfering substituent" are provided, including alkyl (1-6 C), halo, alkoxy (1-6 C), OR, NR_2 , SR, CN, NO_2 , SO_3H , and R, where R is alkyl or an alkenyl optionally substituted by halo, =O, and optionally containing O, S, or N (paragraph 42). A few specific examples of suitable spacers are provided, including CH_2CH_2 , peptide, or polyalkylene glycol (paragraph 40). However, there is uncertainty with regard to the structures of other moieties which may be non-interfering substituents, especially depending on the nature of other variables in the compound, such as the chelating ligand and the length of the $(CH_2)_m$ moiety. There is also no guidance in the specification with regard to structural/functional characteristics of additional compounds such which act as R^1 or the spacer, such as solubility or toxicity properties, for example. The method of making the compounds is only directed to certain R^1 and spacer moieties exemplified, which includes coupling the spacer via standard peptide techniques (example 1). There are a relatively small number of species which are exemplified, especially for the spacer variable, which include only CH_2CH_2 , peptide, or polyalkylene glycol. Because of the wide variety of substituents or spacers available to the skilled artisan, a more detailed description of what is being claimed is necessary to show possession of the invention. For example, the *specific* substituents to represent R^1 and the *specific* chemical moieties to represent the spacer should be described in the independent claim. In sum, the specification does not provide any description of the R^1 and spacer required to make and use the broad compound as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim is confusing because the independent claim is directed to a defined compound, which includes the variable "spacer," yet the comprising language of claim 9, wherein the spacer comprises a peptide or polyalkylene glycol, is open-ended. Such open-ended language indicates further substances may be encompassed in the compound in addition to the peptide or polyalkylene glycol. One of ordinary skill in the art would not be able to be aware of which further substances would be included because no indication of such substances or any characteristics of additional substances is suggested in the specification.

It is noted that claim 9 would be more favorably considered if the term "comprising" were replaced with "is".

Allowable Subject Matter

Claims 1 – 23 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 1st and 2nd paragraphs, set forth in this Office action.

Conclusions

No claims are allowed at this time.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Grant *et al.* (*Magnetic Resonance in Medicine*, 1989, 11, p. 236 – 243) disclose liposomal MRI contrast agents wherein phosphatidylethanolamine is covalently linked to a DTPA chelate ligand, which binds Gd^{3+} ions (page 238). The structure taught by Grant differs from that of applicant by the phenyl- $(CH_2)_{0-3}$ moiety that links phosphatidylethanolamine (or other spacer-phosphatidyl unit) to the chelate ligand.

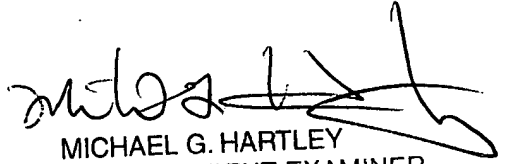
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

lhs



MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER